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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,235	09/25/2006	Stephen Robert Wedge	056291-5302	1868

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MORGAN LEWIS & BOCKIUS LLP
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EXAMINER

NATHAN, SHYAM

ART UNIT	PAPER NUMBER
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4161

MAIL DATE	DELIVERY MODE
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10/03/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,235	Applicant(s) WEDGE, STEPHEN ROBERT	
	Examiner SHYAM NATHAN	Art Unit 4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-24 and 27-34 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 21-24 and 27-34 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/17/2008</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Applicant's election of Group III, claims 21-24 and 27-34, in the reply filed on 09/17/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-16 were previously cancelled, and claims 17-20 and 25-26 are newly cancelled as being directed toward non elected subject matter. Claims 21-24 have been amended to remove their dependency on now-cancelled claims and new claims 31-34 have been added. This is the first Office Action on the merits of the claims.

Priority

Applicant's claim for the benefit of a prior-filed international application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The earliest effective US filing date afforded the instantly claimed invention is 03/22/2005, the filing date of PCT/GB05/01079.

Claim Objections

Claim 29 is objected to because of the following informalities: In line 2, the term -animal-- should appear after "warm-blooded". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

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unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-24 and 27-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10/563439; 10563,440; 10/594,233; 10/594,234; 11,663,912 in view of Lee (US Pub No. 2002/0002162; Pub.Date Jan.3,2002.) The limitation of the claims in the instant application is drawn to AZD2171 combined with a platinum anti-tumor agent. The limitation of the claims of application 10/563439 is drawn to AZD2171 and ZD1839, which is an anti-tumor agent. Lee '162, teaches therapies for treatment of cancer, that further, teach a synergistic method for the treatment of cancer in a mammalian specie[0002,0011] which comprises a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474 [0082], (Also a anti-tumor agent) in conjunction with carboplatin [0079], cisplatin and oxaliplatin [Table 1] (platinum anti0tumor agtents) for the treatment of breast, pancreas, bladder colon lung, skin colorectal, non-small cell lung cancer and mesothelioma.[0059-0067]. Lee also teaches of radiation therapy that

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includes but is not limited to x-rays or gamma rays [0068], that is usually given at the same time as the cancer treating method discussed above. The platinum anti tumor agents (carboplatin, cisplatin, and oxaliplatin) used in the method of Lee '162 can also be added to the VEGF tyrosine kinase inhibitor (AZD2171) of copending Application No. 10/563439. This would be obvious to do so to provide a further cytotoxic agents. Copending applications: 10563,440; 10/594,233; 10/594,234; 11,663,912 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting because their claims can be modified by Lee for the same reasons stated above.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21-24, 27-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (US Pub No. 2002/0002162; Pub. Date Jan. 3, 2002) in light of Hilberg et al. (WO/2004/096224; Prior. date 02/29/2003).

Instant claims 21-24, 27-28 are drawn to a method for the treatment of a cancer involving a solid tumor in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171 (in form of a free base) or a pharmaceutically acceptable salt thereof excluding an AZD2171 maleate salt, before, after or simultaneously with an effective amount of a platinum tumor agent (oxaliplatin, cisplatin, carboplatin) and ionizing radiation.

Lee '162, teaches therapies for treatment of cancer, that further, teach a synergistic method for the treatment of cancer in a mammalian species [0002, 0011] which comprises a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474 [0082], in conjunction with carboplatin [0079], cisplatin and oxaliplatin [Table 1] for the treatment of breast, pancreas, bladder, colon, lung, skin, colorectal, non-small cell lung cancer and mesothelioma. [0059-0067]. Lee also teaches of radiation therapy that includes but is not limited to x-rays or gamma rays [0068], that is usually given at the same time as the cancer treating method discussed above.

But Lee. Does not teach of AZD2171 as a vascular endothelial growth factor receptor tyrosine kinase inhibitor.

Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) teaches of AZD2171 as an vascular endothelial growth factor receptor tyrosine kinase inhibitor(pg.34 lines 1-7)

It would be prima facie obvious to one skilled in the art to substitute the AZD2171 in Hilberg et al. for the ZD6474 taught in Lee '162 because ZD6474 can be substituted for AZD2171 because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action. ZD6474 is taught by itself without a salt being mentioned, therefore, it is a free base. Furthermore, it would be obvious that radiation involving x-rays and gamma rays can be ionising radiation.

Claim 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over : Lee (US Pub No. 2002/0002162;Pub.Date Jan.3,2002 in light of Hilberg et al.(WO/2004/096224;Prior.date 02/29/2003) as applied to claim21-24,27-28 above, and further in view of Lane et al (US Pub No. 2004/0147541; PCT filed 02/18/2002).

Instant claims 29-34 are drawn to a method for the treatment of a cancer involving a solid tumor in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171 salt before ,after or simultaneously with an effective amount of a platinum tumor agent (oxaliplatin,) and ionizing radiation for the treatment of kaposi's sarcoma, colon, brain, thyroid, pancreas, bladder, breast, prostate, lungs, vulva ,skin, colorectal, mesothelioma, small cell lung and lung cancer.

Lee (US Pub No. 2002/0002162; Pub. Date Jan. 3, 2002) teaches of a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474, in conjunction with oxaliplatin, cisplatin, and carboplatin , for the treatment of cancer [0079, Table 1]. And Hilberg et al. (WO/2004/096224; Prior. date 02/29/2003) teaches of AZD2171 as an vascular endothelial growth factor receptor tyrosine kinase inhibitor (pg. 34 lines 1-7) ZD6474 can be substituted for AZD2171 because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action. But Lee does not mention salts of ZD6474 or kaposi's sarcoma.

Lane et al teaches of a method for treating solid tumors [0013], that comprise VEGF receptor tyrosine kinase inhibitors, such ZD6474 [0060], and salts thereof [0073] - (which states that any subject matter relating to compounds in Lane et al., such as pharmaceutically acceptable salts can be incorporated in the Lane et al reference). Lane et al. ,also, comprises oxaliplatin and carboplatin [0058] for the treatment of : **kaposi's sarcoma**, mesothelioma, non small cell lung cancer, colorectal cancer, lung cancer , colon, brain, thyroid, pancreas, bladder, breast, prostate, lungs, vulva , and skin cancer. [0017]

It would be prima facie obvious to one skilled in the art to make the invention taught in Lee in light of Hilberg et al with the invention taught by lane et al. because both Lee and Lane et al. are drawn towards methods for the treatment of cancer and tumors

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that involve VEGF receptor tyrosine kinase inhibitors , such as ZD6474. Furthermore, it would be obvious to one skilled in the art to substitute the salt of a vascular endothelial growth factor receptor tyrosine kinase inhibitors, such as ZD6474, (taught in Lane et al) for the free base form(taught in Lee) and vice versa, and for AZD2171, because they are both vascular endothelial growth factor receptor tyrosine kinase inhibitors, which would give them the same mode of action. Furthermore, Lane et al. in paragraph 0073 discloses that any subject matter relating to the compounds is here incorporated into the application Lane et al. by reference. This includes pharmaceutically acceptable salts, which would include maleate salts of ZD6474.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHYAM NATHAN whose telephone number is (571)270-5753. The examiner can normally be reached on Mon-Thurs 8:30a.m. - 5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SN

/Ashwin Mehta/
Primary Examiner, Technology Center 1600